

Early Postoperative Mortality Following Joint Arthroplasty: A Systematic Review

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ABSTRACT. *Objective.* To perform a systematic review of 30- and 90-day mortality rates in patients undergoing hip or knee arthroplasties.

Methods. Five databases were searched for English-language studies of mortality in hip or knee arthroplasties and the following data were extracted: patient characteristics (age, sex, ethnicity), arthroplasty characteristics (unilateral vs bilateral, hip vs knee), system factors (hospital volume and surgeon volume), year of study, etc. Mortality rates were compared across variable categories; proportions were compared using relative risk ratios and 95% confidence intervals.

Results. Out of 650 titles and abstracts, 80 studies qualified for analysis. Of these, 35%, 34%, and 31% of studies provided 30-, 90-, and > 90-day mortality rates. Overall 30-day mortality rates across all types of arthroplasties were 0.3%; 90-day, 0.7%. For those reports with specific rates, 30-day mortality was significantly higher in men than women [1.8% vs 0.4%, respectively; relative risk (RR) 3.93, 95% CI 3.30–4.68] and in bilateral versus unilateral procedures (0.5% vs 0.3%; RR 1.6, 95% CI 1.49–1.72), but no differences were noted by the underlying diagnosis of osteoarthritis (OA) versus rheumatoid arthritis (0.4% vs 0.3%; RR 0.77, 95% CI 0.48–1.24). 90-day mortality showed nonsignificant trends favoring women, OA as the underlying diagnosis, and unilateral procedures.

Conclusion. Several demographic and surgical factors were associated with higher 30-day mortality rates following knee and hip arthroplasties. More studies are needed to examine the effect of body mass index, comorbidities, and other modifiable factors, in order to identify interventions to lower mortality rates following arthroplasty procedures. (J Rheumatol 2011;38:1507–13; doi:10.3899/jrheum.110280)

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Knee and hip joint replacements are generally successful surgical treatments primarily for patients with osteoarthritis (OA) or rheumatoid arthritis (RA)^{1,2,3}. Hip and knee arthroplasties are generally elective procedures. Those that are nonelective occur following trauma, including fractures, cancers, or joint infections.

While common, nonserious, complications are reported during and after hip and knee arthroplasties, mortality is rare. Due to the elective status of most joint replacements, despite its rarity, estimation and correlates of mortality are nonetheless important to both patients and surgeons. Knee and hip arthroplasties are among the most common elective procedures currently performed in the US, with an increased estimated occurrence by 2030 of 1.5 times for hip and 6 times for knee surgery⁴. Improvements in surgical techniques and sterility have significantly reduced mortality risk. Due to increasing prevalence of these surgeries, it is important to estimate associated mortality rates and their correlates.

One of the main objectives of the Knee and Hip Arthroplasty Special Interest Group (SIG) is to standardize assessment and reporting of benefits and risks of these procedures. In addition to cardiac and thromboembolic complications that may occur in the early postoperative period of arthroplasties, all-cause mortalities are events of extreme importance. One of the first steps in this process is to assess what is important for outcomes reporting from clinical trials

of arthroplasty and whether measures for these outcomes meet the OMERACT filter of truth, discrimination, and feasibility. Death ascertainment is commonly done using National Death Index or reporting of death by family members to a physician practice, and these would meet the filters of truth and feasibility. It is well known that the small sample size and short duration of most clinical trials (which are known limitations of clinical trials) limit the power to detect differences in harms, such as mortality, between interventions. Thus, discrimination ability for mortality may be limited outside the realm of simple, large clinical trials. However, measurement of this outcome is part of every clinical trial for most interventions, due to its inherent importance. This systematic review was designed to estimate risks for the most severe consequences associated with arthroplasties, including immediate postoperative deaths.

The objective was to assess overall mortality rates and their variation according to important characteristics. A systematic review of published studies in the English language of mortality in patients undergoing hip or knee joint replacement was performed, specifically to examine 30- and 90-day mortality rates by patient characteristics [age, sex, race/ethnicity, body mass index (BMI), and comorbidity], surgeon and hospital procedure volume (high/medium/low), hospital type (community center/referral center), setting (US-Canada vs other countries), and type of procedure (total vs partial joint; knee vs hip; primary vs revision). Particular emphasis was placed on 30- and 90-day mortality rates, reasoning that deaths within that timeframe were more likely related to the surgical procedure and immediate postoperative care than those occurring months or years after surgery.

MATERIALS AND METHODS

Literature search and study selection. A librarian performed the literature search on January 9, 2009, using the terms “arthroplasty,” “joint replacement,” or “arthroscopy” and “mortality,” “fatal outcome,” or “death.” The following databases were searched: Cochrane Central Register of Controlled Trials (CENTRAL), via The Cochrane Library, Wiley InterScience (www.thecochranelibrary.com), current issue; OVID Medline, 1966-; CINAHL (via EBSCOHost), 1982-; OVID SPORTdiscus, 1949-; and Science Citation Index (Web of Science) 1945-.

Two reviewers (JK, JAS) independently examined all titles and abstracts. Inclusion criteria were study of mortality in patients with joint replacement; fully published original study in English language, not an abstract, review, or editorial. Consensus was achieved between reviewers. All full-text articles were reviewed by one author (JK), who was trained by the senior epidemiologist (JAS). Publications meeting inclusion criteria were selected, in agreement with the senior author (JAS).

Data abstraction and analyses. For all studies selected for full-text review, data were abstracted (by JK) using a structured data abstraction form. The elements abstracted included study characteristics (study type, type of joint replacement, length of study), setting (country, community hospital vs referral/tertiary hospital), patient characteristics (age, sex, race/ethnicity, BMI, comorbidity), and system characteristics (hospital volume, surgeon volume). Reports that did not provide information regarding elective versus nonelective procedures were considered as including all-comers and were analyzed as such.

Overall 30- and 90-day mortality rates were calculated as the number of

patients who died divided by those at risk (number undergoing arthroplasties). If and when standardized mortality rates were presented, they were extracted. It was anticipated that a small subset of studies would provide mortality rates according to variables of interest. Mortality rates were compared by important patient characteristics (sex), surgery type (primary vs revision; unilateral vs bilateral), and whether surgery was unilateral or bilateral. Realizing that healthcare reimbursement, delivery systems, population health, and access to arthroplasty procedures vary by country, differences between US/Canada and other countries (European countries, Israel, Singapore) were compared as a hypothesis-generating exercise.

Mortality rates were compared between categories of variables using relative risk ratios (calculated using www.pedro.org.au/wp-content/uploads/Ccalculator.xls).

RESULTS

Search strategy and study selection. Search strategy and results are summarized in Figure 1. Of 650 titles reviewed, 145 studies underwent a full review, of which 80 were assessed to have usable data. Of these, 56 (70%) studies summarized data from primary arthroplasty patients, 3 (4%) included those with surgical revisions, and 21 (26%) both. A total of 78 (98%) studies included total joint arthroplasty patients and 2 both total and partial joint replacements. Altogether, 48 studies (60%) summarized only patients with hip arthroplasties, 22 (23%) only knee arthroplasties, and 9 (11%) either knee and/or hip (wrist arthroplasties were excluded, being the only non-hip, non-knee study). The majority included primary arthroplasty procedures: of 48 hip studies, 34 (74%) were primary; 9 reported both knee and hip, 6 (67%) included primary arthroplasties; and of 22 knee studies, 16 (73%) were primary. In the majority of reports, 61/80 (76%), all-comer mortality in subjects undergoing hip or knee joint arthroplasties was reported; few reported mortality in those undergoing elective arthroplasties, 16/80 (20%) or in nonelective procedures, 3/80 (4%).

Overall mortality. Of the 80 studies, 28 (35%) reported 30-day mortality rates, 27 (34%) 90-day rates, and 25/80 studies (31%) > 90-day rates post-procedure. Overall 30- and 90-day postoperative mortality rates across all arthroplasty groups were 0.3% (15,856 per 4,991,811) and 0.7% (4,865 per 651,448), respectively.

Sociodemographic characteristics of patients included in the studies are summarized in Table 1. The majority of patients were Caucasian with an underlying diagnosis of OA; 53%–61% were women, with a mean age of 68 years for both 30- and 90-day mortality estimates.

Association of sex, underlying diagnosis, bilaterality, and type of arthroplasty with 30- and 90-day mortality. A subset of studies provided mortality rates for these variables. Men had significantly higher 30-day mortality rates compared with women (1.8% vs 0.4%, respectively); 90-day rates were similar in men and women (1.1% vs 1.0%; Table 2). As might be expected, bilateral procedures were associated with higher 30-day mortality compared with unilateral arthroplasties (0.5% vs 0.3%; Table 2). However, 90-day mortality did not differ significantly between unilateral and bilateral arthroplas-

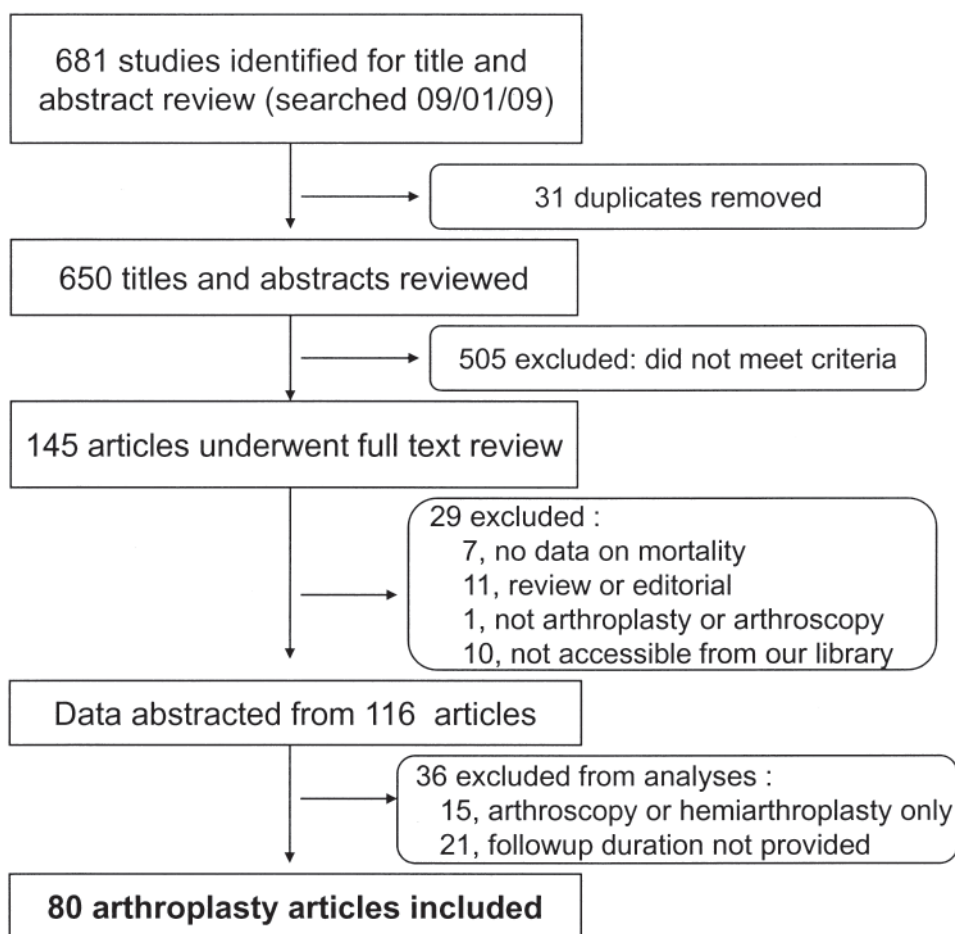


Figure 1. The process of data collection and analysis.

Table 1. Study population characteristics.

Characteristic	30-day Mortality Cohort, mean (SD) or %	90-day Mortality Cohort mean (SD) or %
Mean age (SD), yrs	67.4 (7.0)	68.0 (6.8)
% Female	52.8	61.3
% Caucasian	80.5	91.2
% Osteoarthritis	65.1	82.5
Mean body mass index	28.9 (1.6)	28.1 (2.7)

ty. Data regarding mortality rates according to BMI and associated comorbidities were not included in the reviewed studies, and therefore could not be analyzed.

To determine differences in mortality rates by arthroplasty type, site (knee vs hip) and primary surgery versus revision were analyzed for 30-day (Table 3) and 90-day mortality (Table 4). Pooled 30-day mortality rates were 0.63% for hip and 0.29% for knee arthroplasties (Table 3) and 90-day rates were 0.9% for hip and 0.62% for knee (Table 4). Although some studies reported rates for elective surgery, the majority reported mortality for all-comers (Tables 3 and 4).

Only one study provided data for 30-day mortality rates among subjects undergoing revision arthroplasties and 2 studies reported 90-day mortality rates. Revision procedures were associated with similar 30- and 90-day mortality rates as primary arthroplasties. In subjects undergoing elective procedures, revisions were associated with significantly higher 90-day mortality rates despite significantly lower rates at 30 days (Table 5).

Due to reporting of mortality data by different age categories and lack of studies providing mortality by ethnicity, BMI, or comorbidity, it was not possible to summarize mortality data according to these variables.

Differences by region (US/Canada vs other countries). For all-comers undergoing primary hip and knee arthroplasties, 30-day mortality rates were significantly higher in US/Canada and 90-day rates significantly lower compared with other countries (Table 6).

Analyses for system factors (surgeon volume, hospital volume, setting) and time trends. As there were an insufficient number of studies reporting data by system factors, and the categories were different between studies, these data could not be sum-

Table 2. 30- and 90-day mortality rates by sex, underlying diagnosis, and bilaterality*.

	30-day Mortality		90-day Mortality	
	n/N (%)	Relative Risk (95% CI)	n/N (%)	Relative Risk (95% CI)
Sex				
Female	156/32,612 (0.4)	Reference	382/37,392 (1.0)	Reference
Male	635/33,797 (1.8)	3.93 (3.30–4.68)	195/18,382 (1.1)	1.04 (0.87–1.23)
Underlying diagnosis				
Osteoarthritis	114/31,504 (0.4)	Reference	78/13,686 (0.3)	Reference
Rheumatoid arthritis	20/7,174 (0.3)	0.77 (0.48–1.24)	4/481 (0.8)	1.46 (0.53–4.00)
Laterality				
Unilateral	10,711/3,739,900 (0.3)	Reference	199/28,988 (0.6)	Reference
Bilateral	765/167,069 (0.5)	1.60 (1.49–1.72)	22/2,916 (0.7)	1.13 (0.73–1.76)

* Since only a few studies provided numbers separately for sex, underlying diagnosis, and laterality, the mortality rates may differ from the overall rates, since these studies were a subset of all studies included.

Table 3. 30-day mortality stratified by type of joint (hip vs knee vs both) and type of arthroplasty (primary vs revision vs both)* for elective surgery and all-comers.

	No. Studies**	All Studies Combined (%)	Underlying Indication for Arthroplasty Elective (%)	All-comers† (%)
Hip arthroplasty				
Primary hip	11	2,602/411,675 (0.63)	48/6,703 (0.71)	2,224/352,708 (0.63)
Revision hip††	6		22/7,371 (0.29)	24/2,402 (1.0)
Primary and revision combined	5		90/30,714 (0.29)	234/21,327 (1.1)
Knee arthroplasty				
Primary knee	8	13,233/4,569,617 (0.29)	75/12,108 (0.62)	1,277/372,444 (0.34)
Revision knee††	1		—	4/4,375 (0.1)
Primary and revision combined	7		11,881/4,185,030 (0.28)	0/35 (0)

* Since only a few studies provided numbers separately for knee and hip arthroplasty, the mortality rates may not reflect overall rates, these studies being a subset of all studies included. ** One study could provide data for more than 1 group. † All-comers included studies where all patients were included and those in which there was no clear description of included patients. †† Revision numbers were often a subset of the mortality for the entire sample, frequently with primary arthroplasty constituting a large majority of cohort and high proportion of all deaths.

Table 4. 90-day mortality stratified by underlying type of joint (hip vs knee vs both) and type of arthroplasty (primary vs revision vs both)* for elective surgery and all-comers.

	No. Studies**	Overall (all studies) (%)	Underlying Indication for Arthroplasty Elective (%)	All-comers† (%)
Hip arthroplasty				
Primary hip	2	2,126/236,104 (0.9)	395/46,007 (0.86)	744/100,058 (0.74)
Revision hip††	8		327/15,229 (2.15)	38/3785 (1.0)
Primary and revision combined	6		884/73,750 (1.19)	103/16,289 (0.63)
Knee arthroplasty				
Primary knee	8	2,432/393,540 (0.62)	508/78,745 (0.65)	1,921/313,586 (0.61)
Revision knee††	1		—	1/132 (0.76)
Primary and revision combined	1		—	3/1,209 (0.25)

* Since only a few studies provided numbers separately for knee and hip arthroplasty, the mortality rates may not reflect overall rates, these studies being a subset of all studies included. ** One study could provide data for more than 1 group. † All-comers included studies where all patients were included and those in which there was no clear description of included patients. †† Revision numbers were often a subset of the mortality for the entire sample, frequently with primary arthroplasty constituting a large majority of cohort and high proportion of all deaths.

marized. The surveillance time periods in several studies overlapped more than a decade; therefore time-trend analyses could not be performed.

DISCUSSION

This report presents a systematic review of all published English-language studies including mortality data for patients

Table 5. Comparison of primary and revision arthroplasty for studies including all-comers and elective arthroplasty.

	Primary (%)	30-day Mortality Revision (%)	Relative Risk* (95% CI)	Primary (%)	90-day Mortality Revision (%)	Relative Risk (95% CI)
All-comers	3,501/725,152 (0.5)	28/6,777 (0.4)	0.86 (0.59–1.24)	2,681/415,213 (0.6)	47/6,190 (0.8)	1.18 (0.88–1.57)
Elective	123/18,811 (0.6)	22/7,371** (0.3)	0.46 (0.29–0.72)	1,126/135,496 (0.8)	320/13,128 (2.4)	2.93 (2.59–3.31)

* Relative risk for mortality in the revision arthroplasty with primary arthroplasty as the reference group. ** Data from one study only, with very low mortality risk for revision arthroplasty.

Table 6. 30- and 90-day mortality rates by region.

	US/Canada (%)	30-day Mortality Other Countries (%)	Relative Risk (95% CI)	US/Canada (%)	90-day Mortality Other Countries (%)	Relative Risk (95% CI)
Primary hip: all-comers	893/69,819 (1.28)	1,331/282,889 (0.47)	2.72 (2.50–2.96)	37/8,885 (0.42)	707/91,173 (0.78)	0.54 (0.39–0.75)
Primary knee: all-comers	522/111,385 (0.43)	755/261,059 (0.29)	1.62 (1.45–1.81)	1,733/289,094 (0.60)	188/24,492 (0.77)	0.78 (0.67–0.91)

undergoing elective or nonelective hip or knee arthroplasties. Sociodemographic data of this study population, typical for subjects undergoing knee and hip arthroplasties, included a mean age of 68 years, the majority being women and those with an underlying diagnosis of OA.

In the context of the OMERACT filter, mortality has received little attention, but a renewed focus on safety in the OMERACT and our groups' focus on benefit/risk profiles for arthroplasty should encourage consideration of additional outcomes such as mortality. The current version of the OMERACT filter was designed to assist selection of outcome measures to define efficacy and effectiveness. It is likely that the next version of the filter will take potential risks into account, and thus assessment of outcomes following total joint replacement may assist in this effort.

Certain aspects of mortality assessment require further analyses, i.e., distinguishing between all-cause versus specific-cause mortality, despite the challenges posed by differentiating these in the context of chronic inflammatory diseases. In the absence of a life-threatening condition, the surgical procedure and perioperative stress are partially or mostly responsible for 30- and to some extent 90-day mortality. Nonetheless, explicit definitions regarding specific-cause mortality need to be developed. In future OMERACT work, the focus of this group will be to develop standardized measures of mortality, including comparisons to overall mortality rates adjusted for age and sex, etc. The challenge remains to define the type of mortality; and what is most important to study of a specific condition, and why? Should the focus be on all-cause or specific mortality? Should we focus on early and late mortality or just early mortality? Assigning causality is particularly challenging, since most patients undergoing arthroplasty are elderly and may have multiple underlying conditions, likely to contribute to both early and later mortality. Another challenge will be to determine how mortality fits into the overall risk-

benefit profile, determining number needed to treat versus potentially harm. Another important issue is whether it is possible to assess these differences with traditional sample sizes for arthroplasty trials (300–1500 typically for randomized controlled trials).

Several important observations from these analyses deserve further attention.

First, overall 30- and 90-day mortality rates were 0.3% and 0.7%, respectively. These findings may not facilitate broad generalizations, as studies included patients undergoing knee and/or hip arthroplasties and the majority were performed in the Western hemisphere (USA, Canada, Europe). Nonetheless, summary estimates of mortality will be useful to patients, providers, and policy-makers, as comparative effectiveness becomes increasingly important, and both benefits and potential risks of arthroplasty procedures are compared with other interventions.

Second, men undergoing hip or knee arthroplasties had significantly increased 30-day mortality rates, compared with women. This confirms similar observations from previous arthroplasty studies with large sample sizes, most of which were included in this analysis. Higher prevalence of preoperative cardiac morbidity as well as higher perioperative cardiac complications in men may explain the higher mortality rate, although more data are required to test this hypothesis.

Third, as expected, mortality rates were significantly higher in all-comers undergoing revisions versus primary arthroplasties: likely related to older age, more comorbidities, and surgical complexity. Higher complication rates⁵ and poorer health-related quality of life outcomes^{6,7} have been reported following joint replacement revisions, compared with primary arthroplasty. These are likely reflective of higher comorbidity and poorer general health in revision candidates, and this at least partially explains the higher mortality rate for surgical revision procedures. A lower 30-day mortality rate in elective

revisions compared with elective primary arthroplasty procedures is unexpected; as only one study provided such data, these estimates may not be representative and may change with availability of more data.

Fourth, subjects undergoing bilateral procedures had higher 30-day mortality rates compared with those undergoing unilateral arthroplasties. Because of higher 30-day mortality rates, risks of simultaneous bilateral versus unilateral arthroplasty procedures need to be balanced against their potential benefits. Interestingly, 90-day rates were not significantly different between unilateral versus bilateral procedures. This may be due to the lack of power to detect these differences at 90 days (sample size 80–100 times higher for 30- vs 90-day sample) or the slight increase in higher mortality in the early postoperative period in bilateral cases, relative to unilateral arthroplasty, balanced by similar mortality in the later period (between 30 and 90 days) in patients undergoing arthroplasty, unrelated to laterality (unilateral vs bilateral).

Fifth, no significant differences in mortality rates between OA and RA patients may be due to improved treatment for RA in recent years, which may have reduced disease-associated mortality and comorbidities. However, this finding needs to be interpreted with caution due to the small number of events and small sample sizes of subjects with RA: 20 mortality events among 7,174 at 30 days and 4 events among 481 patients at 90 days.

Another hypothesis-generating observation was the differences in mortality rates between US/Canada and other countries — potentially attributable to differences in the proportion of primary versus revision procedures, variability between healthcare systems, and access to arthroplasty and post-procedure rehabilitation. Future research should focus on determinants of mortality rates across countries, to explain this variability in mortality rates.

Regarding system factors such as surgeon and hospital volume, several studies have found an association between higher procedure volume, better outcomes, lower revision rates^{8,9,10}, and lower mortality⁹. We were unable to summarize data from the included studies since the definitions of low versus high volume differed between studies; however the results favored high-volume hospitals. Since they were reproducible, these results are widely accepted as valid and no additional studies were available to allow metaanalysis.

This study has several strengths and limitations. This was a comprehensive literature search; data were abstracted using standardized methods and analyzed according to important clinical characteristics. Despite a large number of studies, results regarding revision arthroplasties are limited and may have led to type II errors, i.e., missing an important difference due to lack of adequate power. Multivariable-adjusted analyses could not be performed due to small sample size and several candidate variables, due to concern for overadjustment. Thus, these comparisons between crude rates should be interpreted with caution. Additionally, reported studies were of

variable duration, from one week to several months, and a prior decision to analyze mortality rates in categories of ≤ 30 days and ≤ 90 days (clinically meaningful) may have resulted in under- or overestimation. Most studies originated from single or group practices, and although several utilized validated datasets such as Medicare and National Inpatient sample and National Hospital Discharge Summary, the sources of mortality were variable. We doubt that ascertainment of death could vary significantly between studies, but small ascertainment errors are possible. As study sample sizes varied, it is expected that larger studies influenced overall mortality rates more than smaller studies. Another limitation included the relative lack of studies reporting results in nonelective procedures, as well as revision arthroplasties. Analyses by BMI and associated comorbidities could not be performed due to lack of relevant data. We combined US and Canadian populations as compared to other countries for country comparisons, but caution must be exercised interpreting these results, since there are differences in these healthcare systems between countries that we combined. The risk of mortality may differ based on differences in patient selection, comorbidity load, and mortality risk in the general population in each country.

This systematic review quantified mortality rates following hip or knee arthroplasties. Significantly higher mortality rates were noted in men compared to women, revision versus primary, and bilateral versus unilateral procedures. Studies examining associations of BMI and baseline comorbidities with mortality rates have not been reported, despite the fact that many of these factors are modifiable. It is expected that better understanding of the potential role of these factors in overall outcomes will help to reduce mortality in patients undergoing hip or knee arthroplasties. Several questions related to mortality assessment and reporting following arthroplasty remain, such as how to standardize the reporting, what adjustments are needed, how to measure differences, and assessment of cause-specific versus all-cause mortality. Our group plans to address these challenges in future studies.

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